

and wherein the antibody specifically binds to at least one polypeptide selected from the group consisting of the human adenine nucleotide translocator polypeptide, the DLYDDDDK [SEQ ID NO:56] epitope tag and the DYKDDDDK [SEQ ID NO:55] epitope tag.

#### REMARKS

Favorable reconsideration of the subject application is respectfully requested in view of the above amendment and the following remarks. Claims 92-139 are pending in the application, with claims 109-139 standing withdrawn from consideration by the Examiner, without prejudice to prosecution in a related application. Accordingly, claims 92-108 are currently under examination in the application, with claims 92-107 standing rejected, and claim 108 objected to as being dependent upon a rejected base claim, but being otherwise allowable if rewritten in independent form. By the above amendment, claim 107 has been amended, for purposes of clarity and to more particularly set forth Applicants' claimed invention. The amendment and remarks provided herein are not to be construed as acquiescence with regard to the Examiner's rejections, and are made without prejudice to prosecution of Applicants' disclosed subject matter in a related divisional, continuation and/or continuation-in-part application. For the Examiner's convenience, please find appended hereto a complete set of the currently pending claims.

#### REQUEST FOR WITHDRAWAL OF FINALITY OF OFFICE ACTION DATED OCTOBER 21, 2002

As an initial matter, Applicants respectfully request reconsideration and withdrawal of the finality of the Office Action dated October 21, 2002; as elaborated upon hereinbelow, Applicants believe the final rejection is premature.

If, on request by applicant for reconsideration, the primary examiner finds the final rejection to have been premature, he or she should withdraw the finality of the rejection. The finality of the Office action must be withdrawn while the application is still pending. (MPEP 706.07(d))

Applicants respectfully submit that the Final Office Action dated October 21, 2002, by failing to substantively consider and address Applicants' Response filed July 30, 2002, is premature in its finality. More particularly, in the Response filed July 30, 2002, Applicants noted and questioned why the apparent basis for the Examiner's rejections under 35 U.S.C. § 103 relied on alleged teachings of the cited art pertaining to "first energy transfer molecules", "second energy transfer molecules", "MPT" (mitochondrial permeability transition), and the like,

92. (New) A method of identifying an agent that alters binding of an adenine nucleotide translocator polypeptide to a cyclophilin polypeptide, comprising:

(a) contacting, in the absence and presence of a candidate agent, (i) a first isolated recombinant polypeptide comprising a cyclophilin polypeptide or variant thereof with (ii) a sample comprising a second isolated recombinant polypeptide that comprises a recombinant human adenine nucleotide translocator polypeptide or variant thereof, under conditions and for a time sufficient to permit the cyclophilin polypeptide, the adenine nucleotide translocator polypeptide and the candidate agent to interact; and

(b) comparing a level of binding of the first isolated recombinant polypeptide to the second isolated recombinant polypeptide in the absence of the candidate agent to the level of binding of the first isolated recombinant polypeptide to the second isolated recombinant polypeptide in the presence of the candidate agent, wherein a decreased level of binding in the presence of the agent indicates an agent that inhibits binding of an adenine nucleotide translocator polypeptide to a cyclophilin polypeptide and wherein an increased level of binding in the presence of the agent indicates an agent that enhances binding of an adenine nucleotide translocator polypeptide to a cyclophilin polypeptide, and therefrom identifying an agent that alters binding of an adenine nucleotide translocator polypeptide to a cyclophilin polypeptide.

93. (New) The method of claim 92 wherein at least one of the first and second isolated recombinant polypeptides is a fusion polypeptide.

94. (New) The method of claim 92 wherein the first isolated recombinant polypeptide comprises a human cyclophilin D polypeptide that is fused to an additional polypeptide, wherein the additional polypeptide is other than glutathione-S-transferase,

95. (New) The method of claim 92 wherein the cyclophilin polypeptide is selected from the group consisting of human cyclophilin A, human cyclophilin B, human cyclophilin C and human Cyp-60.

Sub Ba 96. (New) The method of claim 92 wherein the first isolated recombinant polypeptide comprises a cyclophilin polypeptide fused to an additional polypeptide that is

selected from the group consisting of polyhistidine, polylysine, a haemagglutinin epitope tag, an XPRESS™ epitope tag, a FLAG® epitope tag, a Myc epitope polypeptide, a FLASH peptide, an immunoglobulin constant region polypeptide, streptavidin, a green fluorescent protein polypeptide, an aequorin polypeptide, a glutathione-S-transferase polypeptide and a *Staphylococcus aureus* protein A polypeptide.

97. (New) The method of claim 92 wherein the first isolated recombinant polypeptide is detectably labeled with a linked reporter group.

98. (New) The method of claim 92 wherein the first isolated recombinant polypeptide comprises a cyclophilin polypeptide fused to an additional polypeptide that is polylysine and the second isolated recombinant polypeptide comprises a recombinant human adenine nucleotide translocator polypeptide fused to an XPRESS™ epitope tag.

91 99. (New) The method of claim 98 wherein the first isolated recombinant polypeptide is detectably labeled with a linked reporter group.

100. (New) The method of either claim 97 or claim 99 wherein the linked reporter group is selected from the group consisting of a radioactive reporter group, a dye, an enzyme, a ligand, a receptor, a protease recognition sequence, a luminescent reporter group and a fluorescent reporter group.

101. (New) The method of claim 92 wherein the sample which comprises the second isolated recombinant polypeptide comprises at least one isolated mitochondrion.

102. (New) The method of claim 92 wherein the sample which comprises the second isolated recombinant polypeptide comprises at least one submitochondrial particle.

103. (New) The method of claim 92 wherein the sample which comprises the second isolated recombinant polypeptide is immobilized on a solid support.

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104. (New) The method of claim 92 wherein the second isolated recombinant polypeptide comprises a human adenine nucleotide translocator polypeptide or variant thereof that is fused to an additional polypeptide selected from the group consisting of polyhistidine, polylysine, a haemagglutinin epitope tag, an XPRESS™ epitope tag, a FLAG® epitope tag, a Myc epitope polypeptide, a FLASH peptide, an immunoglobulin constant region polypeptide, streptavidin, a green fluorescent protein polypeptide, an aequorin polypeptide, a glutathione-S-transferase polypeptide and a *Staphylococcus aureus* protein A polypeptide.

105. (New) The method of claim 92 wherein the step of comparing binding levels comprises detection of a detection reagent that specifically binds to at least one of the polypeptides selected from the group consisting of the first isolated recombinant polypeptide and the second isolated recombinant polypeptide.

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106. (New) The method of claim 105 wherein the detection reagent is an antibody.

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107. (New) The method of claim 106 wherein the second isolated recombinant polypeptide comprises a human adenine nucleotide translocator polypeptide or variant thereof that is fused to a polypeptide selected from the group consisting of an XPRESS™ epitope tag and a FLAG® epitope tag, and wherein the antibody specifically binds to at least one polypeptide selected from the group consisting of the human adenine nucleotide translocator polypeptide, the XPRESS™ epitope tag and the FLAG® epitope tag.

108. (New) The method of claim 92 wherein the first isolated recombinant polypeptide comprises human cyclophilin D and wherein the sample which comprises the second isolated recombinant polypeptide comprises at least one submitochondrial particle isolated from a *T. ni* cell that expresses a recombinant human adenine nucleotide translocator-3 polypeptide fused to an XPRESS™ epitope tag.

109. (New) A nucleic acid expression construct comprising an expression control sequence operably linked to a polynucleotide encoding a mitochondrial permeability transition pore component polypeptide or a variant thereof fused to an additional polypeptide or a